Human Mesenchymal Stem Cells Genetically Engineered to Overexpress Brain-derived Neurotrophic Factor Improve Outcomes in Huntington's disease Mouse Models.

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Public Summary:
Huntington's disease (HD) is a fatal degenerative autosomal dominant neuropsychiatric disease that causes neuronal death and is characterized by progressive striatal and then widespread brain atrophy. Brain-derived neurotrophic factor (BDNF) is a lead candidate for the treatment of HD, as it has been shown to prevent cell death and to stimulate the growth and migration of new neurons in the brain in transgenic mouse models. BDNF levels are reduced in HD post-mortem human brain. Previous studies have shown efficacy of MSC/BDNF using murine MSCs, and the present study used human MSCs to advance the therapeutic potential of the MSC/BDNF platform for clinical application. Double-blinded studies were performed to examine the effects of intrastriatally transplanted human MSC/BDNF on disease progression in two strains of immune suppressed HD transgenic mice: YAC128 and R6/2. MSC/BDNF treatment decreased striatal atrophy in YAC128 mice. MSC/BDNF treatment also significantly reduced anxiety as measured in the open field assay. Both MSC and MSC/BDNF treatments induced a significant increase in neurogenesis-like activity in R6/2 mice. MSC/BDNF treatment also increased the mean lifespan of the R6/2 mice. Our genetically modified MSC/BDNF cells set a precedent for stem cell-based neurotherapeutics and could potentially be modified for other neurodegenerative disorders such as amyotrophic lateral sclerosis, Alzheimer's disease, and some forms of Parkinson's disease.

Scientific Abstract:
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